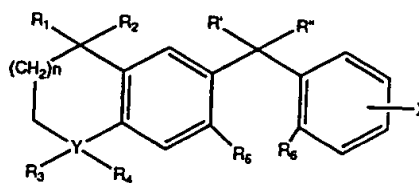


IN THE CLAIMS

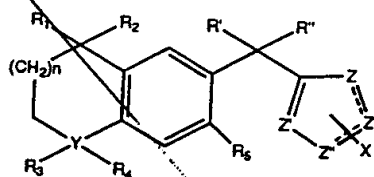
Please cancel claims 1-3 and 33-61 without prejudice.

Please amend claims 4, 15, 19, 21, 22, 23, 27, 29, 30,  
31, 32 as follows:

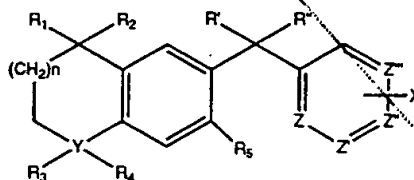
4. (Thrice Amended) A compound having the formula:



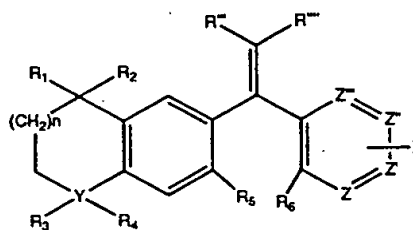
OR

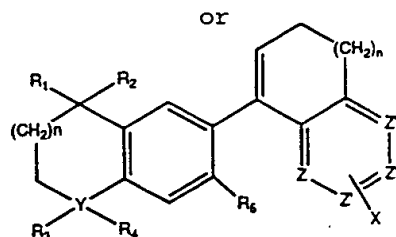


OR

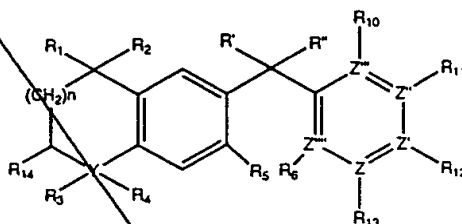


OR

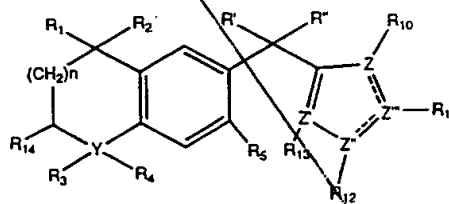




or



or




wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

$Y$  represents C, O, S, N, CHOH, CO, SO,  $SO_2$ , or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is C, but  $R_4$  does not exist if  $Y$  is N, and neither  $R_3$  or  $R_4$  exist if  $Y$  is S, O, CHOH, CO, SO, or  $SO_2$ ;

*sub D*  R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R<sub>7</sub>R<sub>8</sub>)N-N=, R<sub>17</sub>O-N=, R<sub>17</sub>N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R''' and R'''' represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or R''' and R'''' taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

R<sub>5</sub> represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub>, or (CF)<sub>n</sub>CF<sub>3</sub>, but R<sub>5</sub> cannot be hydrogen if [together R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> and R<sub>13</sub> are all hydrogen, Z, Z', Z'', Z''', and Z'''' are all carbon, and] R' and R'' represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or R' and R'' taken together form an oxo, methano, or hydroxyimino group;

*C<sub>1</sub> until* R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub> each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or (CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N, and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

*51*  
*D*  
R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, acyl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

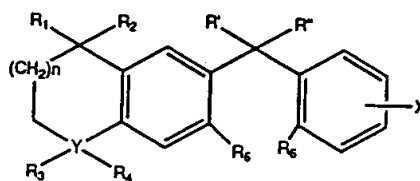
*C1*  
*unsub*  
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

n = 0-3; and

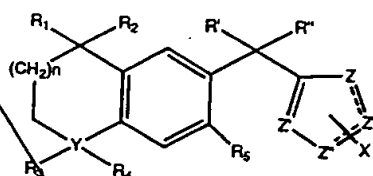
the dashed lines in the second and seventh structures shown depict optional double bonds.

*15*  
*C2*  
15. (Twice Amended) A pharmaceutical composition comprising in a pharmaceutically acceptable vehicle suitable for enteral, parenteral, or topical administration, one or more compounds having the formula:

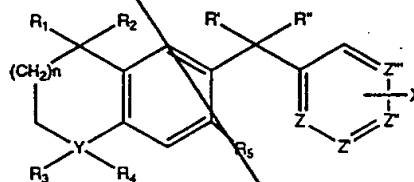
*Sub 3*



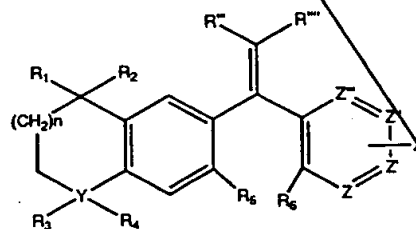
OR



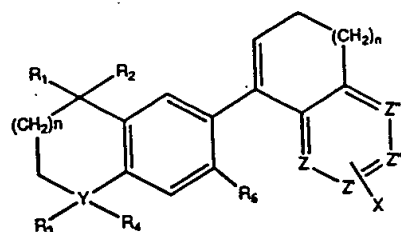
OR



OR

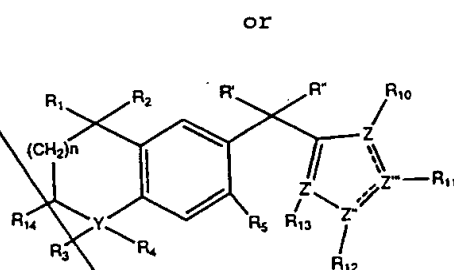
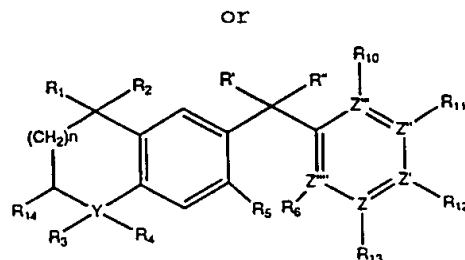


OR



*C2  
contd*

sub  
52



wherein

R<sub>1</sub> and R<sub>2</sub>, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

R<sub>3</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

R<sub>4</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R<sub>4</sub> does not exist if Y is N, and neither R<sub>3</sub> or R<sub>4</sub> exist if Y is S, O, CHOH, CO, SO, or SO<sub>2</sub>;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R<sub>7</sub>R<sub>8</sub>)N-N=, R<sub>17</sub>O-N=, R<sub>17</sub>N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

C1  
could

*sub D2*  
R'" and R''' represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or R'" and R''' taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

R<sub>5</sub> represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub>, or (CF)<sub>n</sub>CF<sub>3</sub>, but R<sub>5</sub> cannot be hydrogen if [together R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> and R<sub>13</sub> are all hydrogen, Z, Z', Z'', Z''', and Z'''' are all carbon, and] R' and R'' represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or R' and R'' taken together form an oxo, methano, or hydroxyimino group;

R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub> each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or (CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N, and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

*C2 contd*  
R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines

*sub D2*  
(including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

*2*  
*cancel*  
n = 0-3; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

*sub D2*  
19. (Twice Amended) A method for modulating a process mediated by one or more Retinoid X Receptors, said method comprising causing said process to be conducted in the presence of at least one compound having the formula:

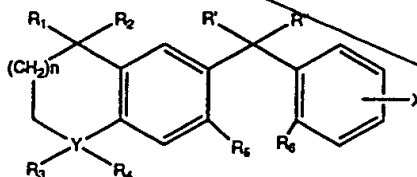
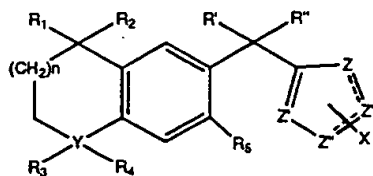


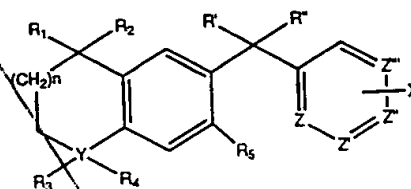


fig 3

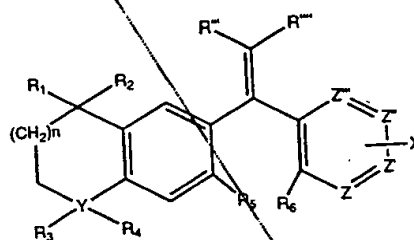
or



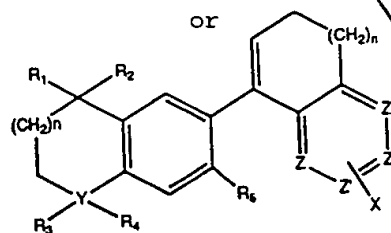
or



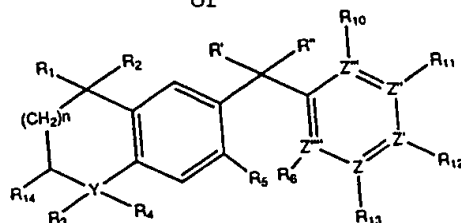
or



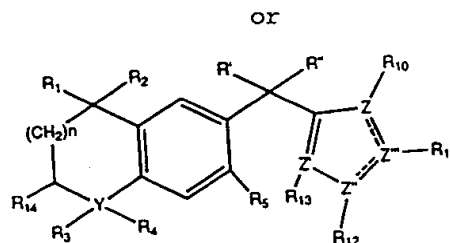
or



or



C3  
contd



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO,  $SO_2$ , or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if [together  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are all hydrogen, Z,

ik  
D3

Z', Z'', Z''', and Z''' are all carbon, and R' and R'' represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or R' and R'' taken together form an oxo, methano, or hydroxyimino group;

R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub> each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or (CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z''' from which it originates is N, and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR<sub>7</sub> and SR<sub>7</sub> substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR<sub>7</sub> and SR<sub>7</sub> substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR<sub>7</sub> and SR<sub>7</sub> substituted alkenes), alkyl amines (including halogen, acyl, OR<sub>7</sub> and SR<sub>7</sub> substituted alkyls), and alkenyl amines (including halogen, alkenyl, OR<sub>7</sub> and SR<sub>7</sub> substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable

C3  
contd

*D3*  
salt when X originates from a C in the 2 or 6 position on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

*C3 would*  
n = 0-3; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

*C4*  
~~18~~ 21. (Twice Amended) A method according to claim 19 wherein said process is the *in vivo* modulation of lipid metabolism, *in vivo* modulation of skin-related processes, *in vivo* modulation of autoimmune diseases, *in vivo* modulation of fatty acid metabolism, *in vivo* modulation of malignant cell development, or *in vivo* modulation of premalignant lesions[, or *in vivo* modulation of programmed cell death].

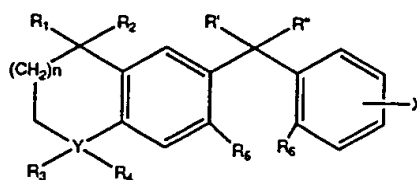
~~22.~~ (Amended) The method according to claim [21] 19 wherein said process is the *in vivo* enhancement of programmed cell death.

*C5*  
~~20~~ 23. (Amended) The method according to claim [21] 19 wherein said process is the *in vivo* inhibition of programmed cell death.

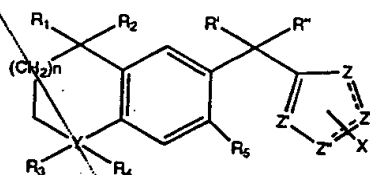
*D4*  
*C5*  
27. (Twice Amended) A method for modulating a process mediated by one or more Retinoid X Receptors, said method comprising administering to a mammalian subject an amount, effective to modulate said process mediated by said one or more

sub  
D4

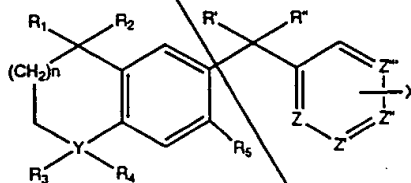
Retinoid X Receptors, of one or more compounds having the  
formula:



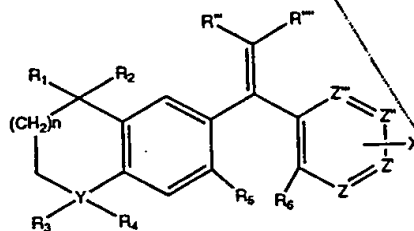
or



or



or



C5  
contd

The chemical structure shows a central benzene ring. At the top-left position, there are two substituents, R<sub>1</sub> and R<sub>2</sub>. At the bottom-left position, there are two substituents, R<sub>3</sub> and R<sub>4</sub>. At the bottom-right position, there is a substituent R<sub>6</sub>. A (CH<sub>2</sub>)<sub>n</sub> chain is attached to the left side of the benzene ring, leading to a Y atom. The Y atom is also bonded to a (CH<sub>2</sub>)<sub>n</sub> chain, which is then connected to a ring system. This ring system includes a double bond and several Z atoms, with one Z atom bonded to an X atom.

CS  
could

R<sub>3</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

24  
54

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if [together  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are all hydrogen, Z, Z', Z'', Z''', and Z'''' are all carbon, and  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N, and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

C5  
contd

44  
DT

R<sub>1</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>2</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>3</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>4</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, acyl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR, COSR, CONHR, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

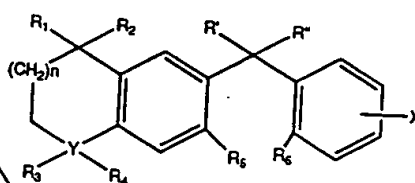
n = 0-3; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

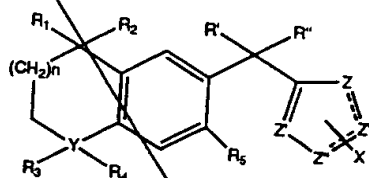
CS  
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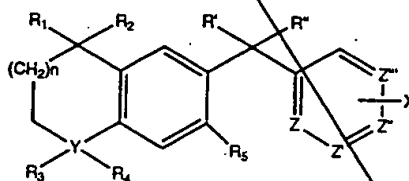
29. (Twice Amended) A method for treating a mammalian subject requiring Retinoid X Receptor therapy comprising administering to such subject a pharmaceutically effective amount of one or more compounds having the formula:



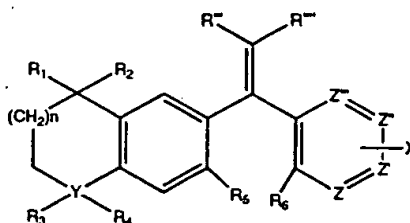
or



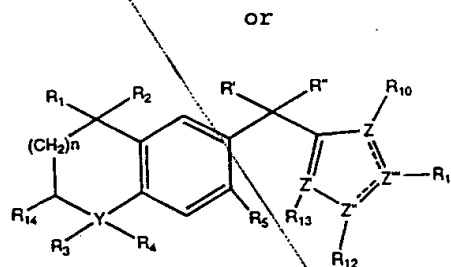
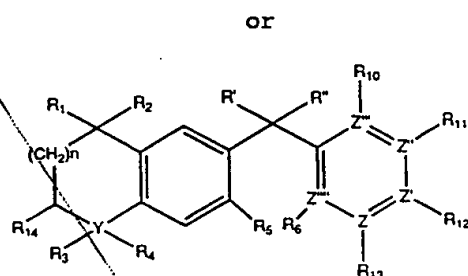
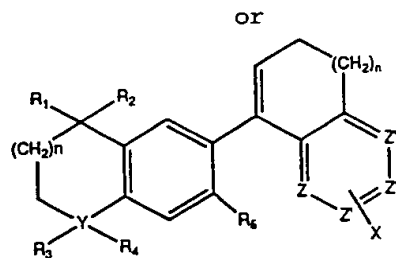
or



or



*Handwritten:* 55



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

$Y$  represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is C, but  $R_4$  does not exist if  $Y$  is N, and neither  $R_3$  or  $R_4$  exist if  $Y$  is S, O, CHOH, CO, SO, or SO<sub>2</sub>;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

*Handwritten:* C6 units

*Handwritten:*  $\frac{R_5}{D}$

or R' or R" taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R<sub>7</sub>R<sub>8</sub>)N-N=, R<sub>17</sub>O-N=, R<sub>17</sub>N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R'" and R''' represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or R'" and R''' taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

R<sub>5</sub> represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub>, or (CF)<sub>n</sub>CF<sub>3</sub>, but R<sub>5</sub> cannot be hydrogen if [together R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> and R<sub>13</sub> are all hydrogen, Z, Z', Z'', Z''', and Z''' are all carbon, and] R' and R" represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or R' and R" taken together form an oxo, methano, or hydroxyimino group;

R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub> each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or (CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z''' from which it originates is N, and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

*Handwritten:* C<sub>6</sub> contd

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

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R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, acyl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

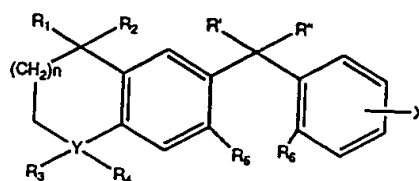
n = 0-3; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

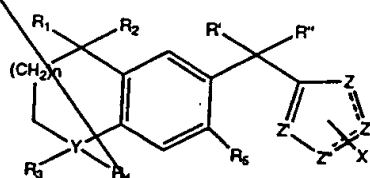
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30. (Twice Amended) A method for increasing plasma concentrations of high density lipoprotein in a mammalian subject comprising administering to such subject a pharmaceutically effective amount of one or more compounds having the formula:

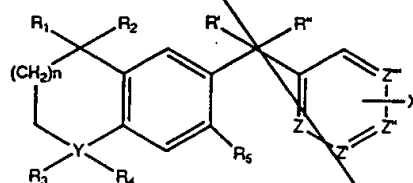
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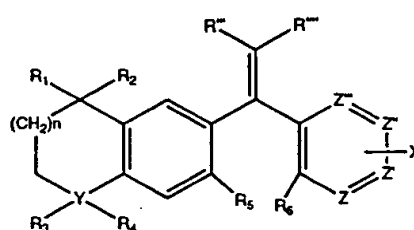
or



or



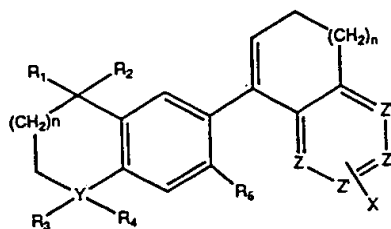
or



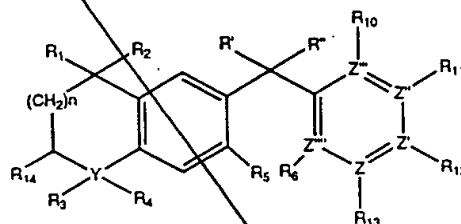
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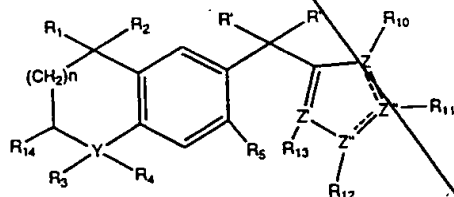
or



or



or



wherein

R<sub>1</sub> and R<sub>2</sub>, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

R<sub>3</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

C4  
contd

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D

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

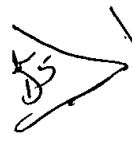
or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if [together  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are all hydrogen, Z, Z', Z'', Z''', and Z'''' are all carbon, and]  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N, and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

45  R<sub>1</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>2</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>8</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, acyl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

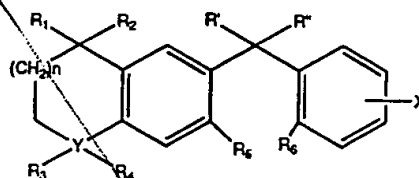
n = 0-3; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

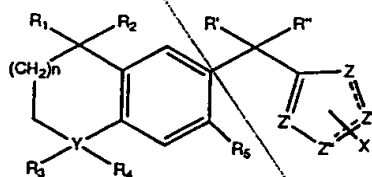


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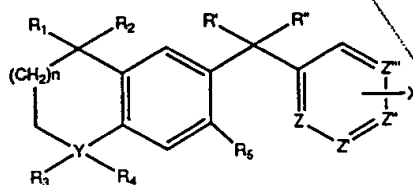
31. (Twice Amended) A method for determining the presence of one or more Retinoid X Receptors comprising combining a compound as set forth below with a sample containing one or more unknown receptors and determining whether said compound binds to any receptor in said sample, said compound having the formula:



OR

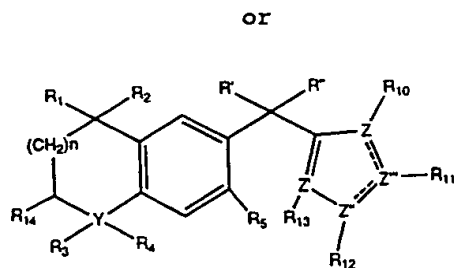
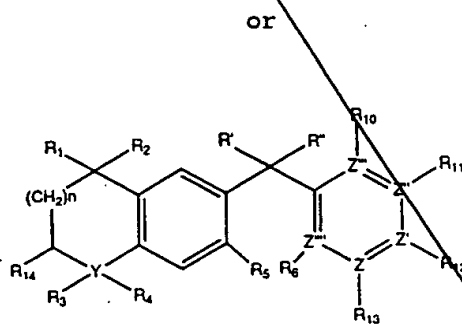
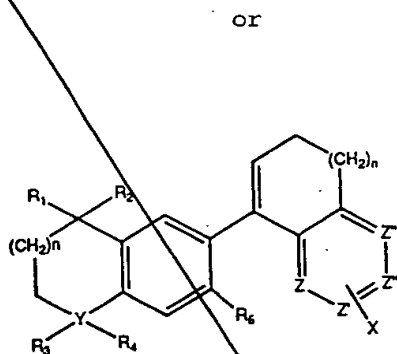
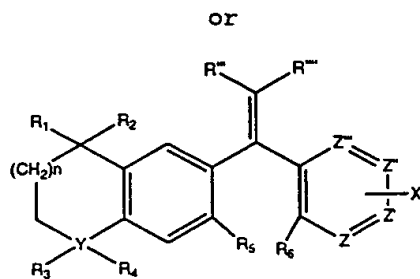


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wherein

R<sub>1</sub> and R<sub>2</sub>, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

R<sub>3</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

R<sub>4</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R<sub>4</sub> does not exist if Y is N, and neither R<sub>3</sub> or R<sub>4</sub> exist if Y is S, O, CHOH, CO, SO, or SO<sub>2</sub>;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R<sub>7</sub>R<sub>8</sub>)N-N=, R<sub>17</sub>O-N=, R<sub>17</sub>N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R''' and R'''' represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or R''' and R'''' taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

C<sub>6</sub>  
could

R<sub>5</sub> represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub>, or (CF)<sub>n</sub>CF<sub>3</sub>, but R<sub>5</sub> cannot be hydrogen if [together R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> and R<sub>13</sub> are all hydrogen, Z, Z', Z'', Z''', and Z'''' are all carbon, and] R' and R'' represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or R' and R'' taken together form an oxo, methano, or hydroxyimino group;

R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub> each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or

A  
D5

(CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N, and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

C6  
until

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to

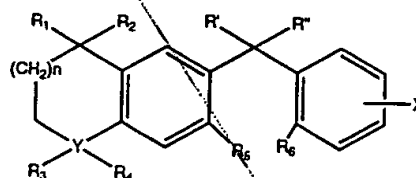
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another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N;

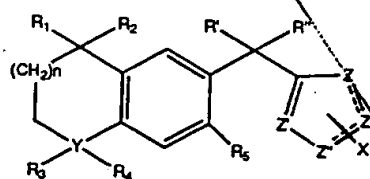
$n = 0-3$ ; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

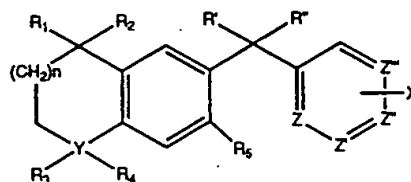
32. (Twice Amended) A method of purifying Retinoid X Receptors comprising combining a compound as set forth below with a sample containing one or more said Retinoid X Receptors, allowing said compound to bind with Retinoid X Receptors, and separating out the bound combination of said compound and Retinoid X Receptor, said compound having the formula:



or



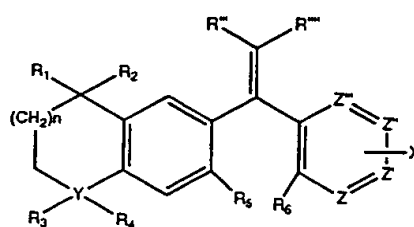
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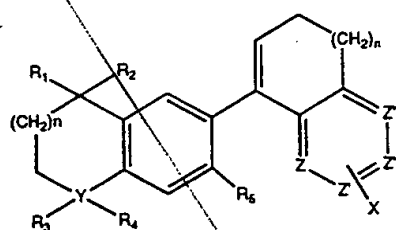
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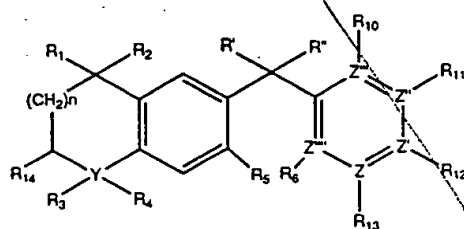
or



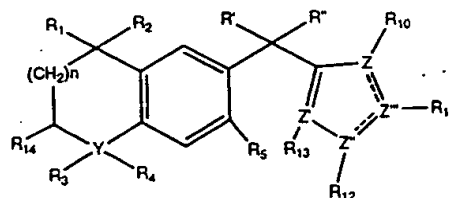
or



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or



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wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or SO<sub>2</sub>;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, ( $R_7R_8$ )N-N=,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub>, or (CF)<sub>n</sub>CF<sub>3</sub>, but  $R_5$  cannot be hydrogen if [together  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  and  $R_{13}$  are all hydrogen, Z, Z', Z'', and Z''' are all carbon, and]  $R'$  and  $R''$  represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or

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(CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z''' from which it originates is N, and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, a[cl]ryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CNO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

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Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to